REMARKS

No claim has been amended. Claims 1-3 and 6-9 remain in the application.

Claim Rejections – 35 U.S.C. §103

Claims 1-3, 6-7 and 9 stand rejected under 35 U.S.C. §103(a) as allegedly being obvious over Van Loef (*High-Energy-Resolution Scintillator: Ce^{3+} Activated $LaBr_3$*) in view of Young (USP 6,297,506). Also, claim 8 stands rejected under 35 U.S.C. §103(a) as allegedly being obvious over Van Loef and Young further in view of Cherry (USP 6,552,348). These rejections are respectfully traversed.

As noted in previous responses, the claims are directed to a PET detector and a corresponding PET scanner and scanning system. The claimed PET detector includes a plurality of photomultiplier tubes arranged with respect to a plurality of scintillator crystals where multiple scintillators provide light output to each photomultiplier tube and where the scintillator crystals and the photomultiplier tubes are arranged respectively peripherally around a cavity for accepting a patient. In exemplary embodiments, the scintillator has a decay time constant $\tau \leq 35$ ns and a light output at least equal to the light output of NaI(Tl). The PET scanning system further includes a time stamp circuit that records the time of receipt of gamma rays by respective PET detectors and provides timing data outputs and a processor that receives the timing data outputs, calculates time-of-flight (TOF) of gamma rays through a patient in the cavity, and uses the TOF of gamma rays in the reconstruction of images of the patient. This configuration simultaneously provides high sensitivity and spatial resolution so as to enable a time-of-flight PET scanning system that has heretofore been unavailable in the art. Such a PET detector and scanning system are not shown or suggested by the references cited by the Examiner.

Van Loef

As evidenced by the title of his article: "High-energy-resolution scintillator: Ce^{3+} activated $LaBr_3$," Van Loef focuses on the energy resolution of the scintillators rather than the timing resolution. In particular, Van Loef emphasizes in the first paragraph of the article the importance of good energy resolution in the application to x-ray astronomy, medical imaging, and gamma ray spectroscopy. Single-photon medical imaging often requires very good energy resolution in order to discriminate photons of different energy, which is clearly a

major attraction of LaBr. Compared to NaI(Tl), the primary scintillator used in single-photon imaging, the energy resolution of LaBr is significantly better (for example, 2.8% vs. 5.6% at 662 keV, as reported in Table 1 by Van Loef). In contrast, PET measures only 511 keV gammas and the need for good energy resolution is less obvious. In fact, BGO has been used in PET for 25 years, is still used commercially by General Electric in their top-of-the-line PET/CT scanners, but it has relatively poor energy resolution.

Van Loef does mention a timing measurement in the third-to-last paragraph of the article. He indicates that a measurement of $LaBr_3$ vs. BaF_2 yields 385 ps. However, this measurement was done using a ^{60}Co source with an energy threshold set at E>800 keV. This may have relevance for x-ray astronomy, but not for PET. Such an experiment presumably measured the timing between two cascade gamma rays, 1.33 MeV and 1.17 MeV, while PET measures the timing between two annihilation 511 keV gamma rays.

As noted in previous amendment responses, Van Loef reported results that demonstrate very good energy resolution and timing resolution. However, these initial measurements were performed with a small crystal (3 x 10 mm) directly coupled to a PMT. A PET detector for TOF requires both very good energy resolution and timing resolution as well as good spatial resolution and high sensitivity. Van Loef does not address the issues of good spatial resolution and high sensitivity needed for time-of-flight PET. For time-of-flight PET, the inventors needed to develop a detector with position encoding (many crystals coupled to a light-guide and array of PMTs as claimed in claims 1-3) using crystals with sufficient length (e.g., 30-mm as claimed in claim 6) so as to achieve good sensitivity for 511 keV gammas while still retaining good energy and timing resolution. Van Loef did not suggest how to do this or even if it could be done, particularly not with $LaBr_3$ or $LaCl_3$ crystals as claimed. The Examiner is again asked to note that the timing response of a crystal configured for a PET application with a narrow aspect ratio (e.g., 4mm x 4mm x 30mm) is very different than that of the crystal used by Van Loef, and the timing resolution of a detector that incorporates light sharing would be expected to be inferior to the configuration described by Van Loef (crystal coupled directly to PMT). As previously noted, Van Loef did not suggest that his crystal could be applied to TOF PET, instead referred to LSO (in the beginning of the article) as being a good candidate for PET because of its higher density.

By contrast, the inventors are able to simultaneously provide high sensitivity (*e.g.*, 30 mm long crystals) and high spatial resolution (*e.g.,* 4 mm wide crystals) by developing a TOF detector which uses many narrow crystals with position encoding - which is possible because $LaBr_3$ or $LaCl_3$ crystals have both high light output and fast timing. Claims 1-3 capture this distinction by claiming that the plurality of photomultiplier tubes are arranged with respect to the plurality of scintillator crystals so that each photomultiplier tube receives light output from several of the scintillator crystals and that the scintillator crystals and the photomultiplier tubes are arranged respectively peripherally around the cavity.

As a result of this configuration for scintillators with very good energy resolution and timing resolution, the necessary sensitivity and spatial resolution for TOF PET become possible. The Examiner has alleged that one of ordinary skill in the art would have used these teachings of Van Loef in conjunction with the teachings of a conventional PET detector by Young to develop such a TOF PET scanner. Applicants respectfully disagree for at least the following reasons.

First, Van Loef did not mention the application of LaBr to PET. Instead, he points out the attraction of LSO for PET (but not TOF PET) in paragraph 2. Applicant submits that there is no indication by Van Loef that $LaBr_3$ or $LaCl_3$ crystals could be used to achieve good timing resolution between 511 keV gamma rays. Since timing resolution depends on the energy of the gamma, the measurement at E>800 keV does not indicate the timing resolution one would achieve at a lower energy. Also, the measurement performed by Van Loef used XP2020Q PMTs which use a UV-transmitting quartz face-plate to allow for the short-wavelength scintillation photons produced by LaBr (maximum emission wavelength = 358 nm, as reported in Table 1). These types of PMTs would not have been used in a PET scanner by one skilled in the art as they are impractical and very costly.

Second, timing resolution also depends on the dimensions of a crystal and the way in which the light is shared among multiple PMTs. Van Loef made his measurement with a small crystal (3 x 10 mm) coupled directly to a PMT. In addition, the measurement by Van Loef was performed at a high energy (1.17 MeV vs. 1.33 MeV) with special-purpose PMTs, as mentioned above. For TOF PET , one measures timing between two 511 keV gamma rays, using very long and narrow crystals (4-mm wide by 30-mm long), and with a light-guide to

distribute the light to multiple PMTs (without quartz face-plates). All of these factors tend to degrade the timing resolution compared to the measurement reported by Van Loef. While there have been PET scanners built with many crystals in a ring with PMTs and light-guides, it was not obvious that one could do this with $LaBr_3$ or $LaCl_3$ crystals and still get very good timing resolution needed for TOF. Certainly, Van Loef provides no such teaching.

Third, while the Examiner acknowledges that Van Loef does not disclose a plurality of photomultiplier tubes and scintillator devices arranged in a PET detector where the scintillator crystals and PMTs are arranged around the periphery of the cavity where a patient is accepted as claimed, the Examiner turns to the patent to Young for such teachings. The Young patent does not address the shortcomings in the teachings of Van Loef. On the contrary, the Young patent describes a method to reduce pile-up errors in PET scanners using two layers of crystals, each with a different decay time. This type of detector is commonly referred to as a phoswitch detector. The example used was a detector with one layer of NaI(Tl) (slower decay = 230 ns) and one layer of LSO (faster decay = 40 ns). This type of scanner could be used for single-photon imaging or for PET imaging, but NOT for TOF PET. The Examiner refers to Figure 2, stating that the processor (element 50) receives the timing data outputs and calculates TOF of the gamma rays, using the TOF for the reconstruction (element 80). This analysis is incorrect. The time stamp circuit in Figure 2 of Young is a generic coincidence timing circuit used in every PET scanner (since one must identify a coincidence between two 511 keV gammas), but does not record the precise time difference between the two gamma rays.

Fourth, the Examiner implies that it is obvious that LaBr, whose basic properties are described in Van Loef, could be developed into a TOF PET scanner by following the teachings of Young, who describes a multi-crystal scanner with two layers of different scintillators. Applicant notes that neither reference mentions TOF PET and that it would not have been obvious to one skilled in the art to have taken the measurements reported by Van Loef and to assume that one could achieve the requisite timing performance needed for TOF PET. Compared to Van Loef's work, for TOF PET performed by the claimed invention uses the timing measurement at a different energy (511 keV), different PMT type (not quartz face-plate), different detector configuration (multiple crystals coupled through a light-guide to

array of PMTs), and different crystal dimensions (4-mm wide by 30-mm long). The fact that this type of arrangement works for conventional (non TOF) PET does not imply that it would work for TOF PET. The Examiner's suggestions to the contrary are unsupported by the cited prior art teachings.

For the foregoing reasons, Van Loef and Young together would not have suggested the claimed PET detector, scanner or scanning system with the claimed configuration so as to enable TOF PET. The Examiner's suggestions to the contrary are unsupported by the cited prior art. Withdrawal of the rejection of claims 1-3, 6-7, and 9 over Van Loef and Young is respectfully requested.

Cherry

Cherry is cited only with respect to claim 8 for the purported teaching of a light guide between the PMT and scintillator crystals for optical coupling. The Examiner is asked to note that neither the scanner configuration nor detector taught by Cherry is suitable for TOF, so even if one would have been motivated to combine the teachings of Cherry with Van Loef and/or Young, the afore-mentioned shortcomings in the teachings of Van Loef and Young would not be overcome. Withdrawal of the rejection of claim 8 over Van Loef, Young and Cherry is respectfully solicited.

Conclusion

The invention of amended claims 1-3 and 6-9 is not shown or suggested by the cited prior art. The present application is thus believed to be in condition for allowance. A Notice of Allowability is respectfully solicited.

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